REMARKS

Entry of the foregoing and reexamination of the above-identified application is respectfully requested.

A clean copy of amended claims 3-5 was requested by the Examiner. Since these claims are being amended in the instant paper, a clean copy of the claims as now of record is provided herein.

The specification remained objected to as the SEQ ID NOs of the May 12, 2000 Sequence Listing do not correlate with the SEQ ID NOs defined in pages 1-4 of the April 16, 2000 response. The appropriate pages in the specification have been amended. Withdrawal of this objection is respectfully requested.

Claims 1-7, 9-11, 16-19 and 20-24 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. This rejection is respectfully traversed.

The Official Action states that the specification is enabling for the plant 5GT protein of SEQ ID NOs: 7 and 9, encoding the plant 5GT protein of SEQ ID NOs: 8, 10 and 12. However, the specification allegedly does not enable any expressed gene which transfers a glycoside to the 5 position of a flavonoid, or any isolated gene or a nucleotide sequence that hybridize thereto, or its complementary strand, coding for a protein having 5GT activity or homologous sequences having 30-50% amino acid identity with SEQ ID NO: 8, 10 or 12, or a modified protein thereof.

Regarding applicants' statement in the prior Response that, based upon the high degree of homology of 5GT proteins between different species one skilled in the art could identify and clone additional genes, the Official Action asserts that there is no evidence that genes obtained by hybridization will encode a functional protein since no specific primers for 5GT genes are disclosed. It is further asserted that without a means to eliminate inoperable embodiments, isolating and screening all proteins encoding 5GT genes is an "invitation to experiment." These assertions are believed to be in error.

More than 500 flavonoids, the position 5 of which is glycosylated, which are present in more than 500 species, are known. *See,* enclosed pages from Jeffrey B. Harborne FRS and Herbert Baxter (Eds.), *The Handbook of Natural Flavonoids*. No undue experimentation would be required for a person having ordinary skill in the art to clone DNAs encoding various flavonoids using as a primer or a probe DNAs described in the specification. As taught in the specification, there is a significant degree of homology between the different species in the amino acid sequence of the protein. For example, interspecies homology is 50% or more, while homology within the same species is 90% or more. *See,* page 7, lines 15-28. Due to the high degree of homology, the information provided in the instant application would enable one skilled in the art to identify additional species without undue experimentation.

Therefore, using the cDNAs provided by applicants, additional genes having the same activity could be readily identified by a person skilled in the art. Screening the proteins encoded by such genes for glycosylation activity would not require undue

experimentation but would be well within the skill of the art. No undue experimentation would thus be necessary.

Broun et al and Lazars et al are cited in the Official Action as allegedly showing that the claimed modifications of the enzymes by addition, deletion and/or replacement of amino acids may result in loss of enzyme activity. However, it is well known in the art that an enzyme molecule comprises regions involving enzyme activity and regions not essential for enzyme activity. Modification in the regions of non-essential amino acid regions may maintain the activity. One skilled in the art can readily compare the amino acid sequences and determine which regions have high degree of identity and thus not make modifications in those identifying sequences.

Regarding claim 21, this claim is directed to the nucleic acid molecules selected from the specific species of Perilla, torenia, verbena and petunia. These are the species for which nucleic acid and amino acid sequences are specifically described in the specification. As described in the specification, within the same species, the homology is 90% or more. One skilled in the art can readily identify additional nucleic acid molecules having such a high degree of homology using the sequences disclosed in the specification. At the very least, this claim should thus be found enabled. One skilled in the art could readily clone additional DNA within the scope of the claim by hybridization with the disclosed DNA of the specification.

Withdrawal of the rejection is thus respectfully requested and believed to be in order.

Claims 1, 6, 7, 9-11, 20, 21 and 23 have also been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification. This rejection is respectfully traversed.

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *In re Kaslow*, 217 USPQ 1059, 1076 (Fed. Cir. 1983); *Ex parte Remark*, 15 USPQ2d 1498, 1506 (PBAI 1990). Given the description in the application of the genus of genes, the particular cDNAs described and the ability of one skilled in the art to use the information provided to identify additional genes, as discussed *supra*, it is respectfully believed that the application would describe the invention as claimed to a person skilled in the art. This information would also convey to the skilled artisan that the inventors had possession of the invention as claimed.

Contrary to the assertion in the Official Action, this situation is not analogous to that in *University of California v. Eli Lilly and Co.* In particular, in *Lilly*, there was no disclosure of the degree of homology between the different species for the given sequence. The instant specification, as discussed *supra*, identifies the high degree of homology both between different species and for the same species for the 5GT gene and protein encoded by same. *See*, page 7, lines 15-28.

Applicants' need not exemplify each member to show possession of the claimed genus. *Utter v. Hiraga* , 845 F.2d 993, 998-99, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Lilly*, 43 USPQ2d at 1406. Applicants identify several different DNA and amino acid sequences for the 5GT gene and protein encoded by same. The high degree of homology within a species and between species is also described. The specification further states:

> Furthermore, although the present specification describes transferases derived from Perilla, verbena, torenia and petunia wherein the transferases that transfer glycoside to the 5 position of a flavonoid (which may be simply referred to as "glysosyltransferase" in the present invention), a gene that codes for said enzyme can be cloned, by entirely or partially altering the purification method of said enzyme so as to purify a glycosyltransferase to another plant, and determining the amino acid sequence of said enzyme. Moreover, by using cDNA of the glycosyltransferase derived from Perilla of the present invention as a probe, cDNA of a different glycosyltransferase was able to be obtained from Perilla, and cDNA of a different glycosyltransferase was able to be obtained from a different plant. Thus, other glycosyltransferase genes can be obtained by using a portion or the entirety of a glycosyltransferase gene.
>
> In addition, as indicated in the present specification, by purifying glycosyltransferase from Perilla, verbena, torenia and petunia to obtain antibody to said enzyme in accordance with standard methods, cDNA or chromosomal DNA produces protein which reacts with that antibody that can be cloned. Thus, the present invention is not limited to only genes of glycosyltransferases derived from Perilla, verbena, torenia and petunia, but also relates to glycosyltransferase in the broad sense.

Page 9, line 37 - page 10, line 25.

The specification thus describes the full scope of the claims and shows that applicants were in possession of the genus as instantly claimed. A means for obtaining the full genus encompassed by the claims is also described.

As noted in applicants' prior response, claims 20-23 parallel the language of claims 1-5 and 7 in Brugliera et al, U.S. Patent No. 5,859,334. Brugliera et al describes only one full length 3 RT sequence in the specification. Based upon this one sequence, claims encompassing a genus of 3RT nucleic acid and DNA molecules were patented. If Brugliera et al's one sequence describes the broader genus, then at the very least applicants' claimed genuses of claims 20-23 are described by the 5 different DNA sequences provided in applicants' disclosure.

Withdrawal of the rejection is respectfully requested and believed to be in order.

Claims 1-7, 9-11 and 16-19 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

The claims have been amended to correct any inadvertent errors. For example, the SEQ ID designations as "amino acid" verses "nucleotide" have been corrected where necessary, e.g., in claims 2-5 and 22-24.

Regarding the recitation of "gene" in the claims, this has been amended as helpfully suggested by the Examiner to recite an isolated "DNA." The phrase "% homology" has been amended to recite "sequence identity" as also suggested by the Examiner. The recitation of "can be hybridized to" has been amended to recite that it is "hybridized."

Regarding the recitation of "identical properties," the claims have been amended to recite that the progeny or tissues conserve the DNA which was introduced.

Claim 20 has been amended as helpfully suggested by the Examiner.

With respect to "breeding" in claim 9 [not 19], this term is not indefinite. "Breeding" is a term of art used for plant cells, similar to the use of "culturing" for microorganisms. Like culturing, the use of breeding without additional steps is correct and is sufficiently definite. One skilled in the art would understand the term as used in the claim.

The breeding and culturing steps are described in the application and need not be recited in the claim because the claims are read in light of the specification. Under 35 U.S.C. §112, second paragraph, a specification shall include claims "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Determining whether a claim is indefinite requires an analysis of "whether one skilled in the art would understand the bounds of the claim when read in light of the specification.... If the claims read in light of the specification reasonably apprize those skilled in the art of the scope of the invention, [section] 112 demands no more." *Credle v. Bond*, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). In the instant application, this standard has been met.

Claims 2-5 and 24 have been amended to correct the inadvertent error in sequences listed. The claims now are sufficiently clear in reciting DNA versus amino acid sequences. The claims inadvertently referred to the original Sequence Listing numbers rather than those from the Sequence Listing filed in May 2001.

With respect to claim 24, this claim has been amended to recite that the DNA sequence hybridizes with the complementary strand of a DNA sequence of SEQ ID NOs: 1, 3, 5, 7 or 11.

In view of the above, withdrawal of the rejection of the claims under §112 is respectfully requested. Such action is believed to be in order.

Claims 20-23 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Brugliera et al. This rejection is respectfully traversed.

Brugliera et al is directed to an isolated nucleotide sequence encoding a petunia 3RT protein. By contrast, the claimed invention is directed to the 5GT protein, and nucleotide/DNA sequence encoding same. The sequence of Brugliera et al does not fall within the scope of the instant claims. Brugliera et al describes the 3RT protein, not the 5GT protein of applicants' invention. Claims 20-23 require the nucleic acid, or a complementary sequence, to encode a plant 5GT protein. Brugliera et al does not disclose or suggest such a nucleic acid since it discloses only the 3RT protein. This is confirmed in *Plant J.* 5:81-92 (1994), a copy of which is enclosed herewith. The 3RT protein does not encode and is not complementary to a sequence encoding, the 5GT protein.

With respect to claim 23, the sequence must (i) encode a 5GT of plant origin as well as (ii) hybridize to a sequence of SEQ ID NOs: 1, 3, 5, 7 or 11, or to a complementary strand thereof. Since Brugliera et al is unrelated to 5GT, it cannot possibly anticipate the claimed sequence. Whether the sequence would hybridize is irrelevant since the claim also requires that the sequence encodes the 5GT protein.

Withdrawal of this rejection under §102(b) is thus respectfully requested. Such action is believed to be in order.

Claims 1-7, 9-11 and 16-19 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Brugliera et al (U.S. Patent No. 5,859,334) in view of Jonsson et al and Sambrooke et al. This rejection is respectfully traversed.

The Official Action states that the prior argument that none of the cited references teach a 5GT gene are not persuasive "because the claims are not limited to specific sequences of 5GT genes ..." The Official Action, however, ignores the fact that all of these claims require that the DNA be "coding for a protein having activity that transfers a glycoside to the 5 position of a flavonoid." *See,* claim 1. There must, therefore, be a disclosure or suggestion of a DNA coding for a 5GT protein.

Brugliera et al, as stated *supra*, does not contain such a disclosure or suggestion. Brugliera et al teaches only the 3RT gene. The Official Action asserts that "[i]n column 3, lines 30-36 Brugliera suggests a nucleotide sequence complementary to a nucleotide sequence encoding a 5GT; homologous sequences of the disclosed 3RT sequences; in columns 7-8, protein mutations comprising amino acid substitution, additions, and/or deletions are also disclosed." Page 11. However, the sole reference to 5GT is the statement that the "invention" is directed to "an isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a plant glycosyltransferase selected from the group consisting of a flavonoid-5-glucosyltransferase (5GT) and anthocyanidin-3-glucoside rhamnosyltransferase (3RT) or a functional part or

derivative of said glycosyltransferase." In the forty-column patent, this is the *only* "disclosure" relating to the 5GT protein. The entirety of the patent is instead directed to the 3RT protein. The mere mention of the 5GT protein without more, however, is hardly an enabling disclosure suggesting the claimed isolated DNA. This in no way describes an isolated DNA coding for a protein having activity that transfers a glycoside to the 5 position of a flavonoid, as recited in applicants' claims.

Moreover, the amino acid identity between the 3RT of Brugliera et al and the 5GT of the instant invention is only 23% for Perilla, torenia and verbena, and only 26% for petunia. It is impossible for one skilled in the art to clone a DNA using conventional hybridization techniques using a probe if the sequence identity between the DNA to be cloned and the probe is only 23% or 26%.

Jonsson et al describes a partially purified anthocyanin 5-O-glucosyltransferase. However, the reference does not describe a purified enzyme or even a partial amino acid sequence. Nor would the information in Jonsson et al provide one skilled in the art with sufficient information that could be used to isolate a DNA or nucleic acid as now claimed. Without even a partial amino acid sequence, it would have been very difficult for a person skilled in the art to clone the isolated DNA of the instant invention based upon the description in Jonsson et al.

Sambrooke et teaches only methods of cloning, isolating and sequencing of genes or cDNAs, and does not teach anything regarding the DNA encoding a 5GT protein.

The combination of references thus fails to disclose or even suggest the claimed invention. As stated *supra*, the mere mention of a nucleic acid encoding 5GT in Brugliera et al is not an enabling disclosure. Nor is the combination of Brugliera et al with Jonsson et al an enabling disclosure. Neither reference teaches anything regarding the nucleotide sequence of a DNA encoding 5GT. Nor does this combination describe the isolation of such a DNA. Only the 3RT protein is isolated in Brugliera et al, while only a partially purified enzyme is described in Jonsson et al. The addition of Sambrooke et al to this combination adds nothing since Sambrooke et al discloses only general cloning, isolating and sequencing methods. As stated *supra*, the 3RT of Brugliera could not have been used to clone a 5GT protein as claimed since the degree of sequence identify is too low. Jonsson et al does not provide sufficient information.

Moreover, if the DNA encoding an isolated 5GT would have been obvious based upon the general statement in Brugliera et al in combination with the teachings of Jonsson et al and Sambrooke et al, it would be assumed that Brugliera et al would have included more information rather than just the simple statement identifying 5GT as being part of the "invention." That nothing else was included is evidence that the instant invention was not obvious at that time, or years later when applicants' invention was made.

Withdrawal of the rejection of record is thus respectfully requested and believed to be in order.

Further and favorable action in the form of Notice of Allowance is respectfully requested. Such action is believed to be in order.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney be telephone at 508-339-3684 so that prosecution would be expedited.

Respectfully submitted,

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Attachment to Reply and Amendment dated April 3, 2002

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Page 5, Paragraph Beginning at Line 37

Examples of the DNAs of the present invention include that which codes for the amino acid sequence described in any one of SEQ ID NOs: 2, 4, 6, [through] 8 or 12. However, proteins having an amino acid sequence modified by addition and/or deletion of one or more amino acids and/or substitutions by one or more other amino acids are also known to maintain enzymatic activity similar to the original protein. Thus, genes coding for a protein that has an amino acid sequence modified by addition and/or deletions of one or more amino acids an/or substitutions by one or more other amino acids relative to the amino acid sequence described in any one of SEQ ID NOs: 2, 4, 6, [through] 8 or 12, and still maintains activity of transferring a glycoside to the 5 position of a flavonoid, also belong to the present invention.

Attachment to Reply and Amendment dated April 3, 2002

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Page 6, Paragraph Beginning at Line 15

The present invention also relates to a gene coding for a protein which gene hybridizes to a nucleotide sequence described in any one of SEQ ID NOs: 1, 3, 5, [through] 7 or 11, or to a nucleotide sequence that codes for an amino acid sequence described therein or to their portions, for example a portion coding for at least six amino acids of a consensus region, under conditions of 2 to 5 x SSC, and for example, 5 x SSC, and 50°C, and that has activity of transferring a glycoside to the 5 position of a flavonoid. Furthermore, the optimum hybridization temperature varies according to the nucleotide sequence and its length, and it is preferable that the hybridization temperature be lower the shorter the nucleotide sequence. For example, a temperature of 50°C or lower is preferable in the case of a nucleotide sequence (18 bases) coding for six amino acids.

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Page 7, Paragraph Beginning at Line 1

Moreover, the present invention also relates to a gene coding for a protein having an amino acid sequence having homology of 30% or more, preferably 50% or more, for example 60% or 70% or more, and in some cases, 90% or more relative to an amino acid sequence of any of SEQ ID NOs: 2, 4, 6, [through] 8 or 12, and having activity that transfers a glycoside to the 5 position of a flavonoid. Namely, as indicated in Example, DNA coding for the enzyme of the present invention demonstrates homology of 20 to 30% in comparison with other glycosyltransferase genes. Thus, the present invention includes genes coding for a protein that having homology of 30% or more with an amino acid sequence described in any one of SEQ ID Nos: 2, 4, 6, [through] 8 or 12, and has glycosyltransferase activity.

Attachment to Reply and Amendment dated April 3, 2002

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Page 7, Paragraph Beginning at Line 15

In addition, as is clear from a comparison of the results of Examples 1 through 4, the amino acid sequence of the enzyme of the present invention varies according to the species, with interspecies homology being 50% or more (see Examples 3 and 4), and for example 60 to 70% (see Example 2), while the homology of the amino acid sequences of the enzymes derived from the same species is 90% or more (see Example 1). Thus, genes coding for a protein that has an amino acid sequence having homology of 50% or more, for example 60-70% or more, and in some cases, 90% or more, relative to an amino acid sequence described in any one of SEQ ID NOs: 2, 4, 6, [through] 8 or 12, and maintains the glycosyltransferase activity of the present invention are included in the present invention.

Attachment to Reply and Amendment dated April 3, 2002

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Page 8, Paragraph Beginning at Line 26

Alternatively, the protein can be obtained by using antibody to an amino acid sequence described in any one of SEQ ID NOs: 2, 4, 6, [through] 8 or 12.

Attachment to Reply and Amendment dated April 3, 2002

Marked-up Claims 1-6, 10, 11, 16-20 and 22-24

1. (Twice Amended) An isolated [gene] DNA coding for a protein having activity that transfers a glycoside to the 5 position of a flavonoid.

2. (Twice Amended) A [gene] DNA as set forth in claim 1 that codes for a protein having an amino acid sequence as shown in any one of SEQ ID NOs: [7 through 10 or 12] 1, 3, 5, 7 or 11 and having activity that transfers a glycoside to the 5 position of a flavonoid, or a protein having an amino acid sequence modified by addition and/or deletion of one or more amino acids and/or substitutions by one or more other amino acids relative to said amino acids and maintains activity that transfers a glycoside to the 5 position of a flavonoid.

3. (Amended) A [gene] DNA as set forth in claim 1 that codes for a protein having an amino acid sequence that has [homology] a sequence identity of 30% or more with an amino acid sequence as shown in any one of SEQ ID NOs: [7 through 10 or 12] 1, 3, 5, 7 or 11, and has activity that transfers a glycoside to the 5 position of a flavonoid.

4. (Amended) A [gene] DNA as set forth in claim 1 that codes for a protein having an amino acid sequence that has [homology] a sequence identity of 50% or more with an amino acid sequence as shown in any one of SEQ ID NOs: [7 through 10 or 12] 1, 3, 5, 7 or 11, and has activity that transfers a glycoside to the 5 position of a flavonoid.

Attachment to Reply and Amendment dated April 3, 2002

Marked-up Claims 1-6, 10, 11, 16-20 and 22-24

5. (Amended) A [gene] DNA as set forth in claim 1 that codes for a protein, wherein said gene [can be hybridized] hybridizes under conditions of 5 x SCC and 50°C with all or a portion of a nucleotide sequence that codes for an amino acid sequence as shown in any one of SEQ ID NOs: [7 through 10 or 12] 1, 3, 5, 7 or 11, and has activity that transfers a glycoside to the 5 position of a flavonoid.

6. (Twice Amended) A vector containing a [gene] DNA as set forth in claim 1.

10. (Twice Amended) A plant into which is introduced a [gene] DNA as set forth in claim 1, or its progeny or tissue [having identical properties] that conserve said DNA which was introduced.

11. (Amended) A cut flower of the plant as set forth in claim 10 or its progeny [having identical properties] that conserve said DNA which was introduced.

16. (Amended) A plant into which is introduced a [gene] DNA as set forth in claim 2, or its progeny or tissue [having identical properties] that conserve said DNA which was introduced.

Attachment to Reply and Amendment dated April 3, 2002

Marked-up Claims 1-6, 10, 11, 16-20 and 22-24

17. (Amended) A plant into which is introduced a [gene] DNA as set forth in claim 3, or its progeny or tissue [having identical properties] that conserve said DNA which was introduced.

18. (Amended) A plant into which is introduced a [gene] DNA as set forth in claim 4, or its progeny or tissue [having identical properties] that conserve said DNA which was introduced.

19. (Amended) A plant into which is introduced a [gene] DNA as set forth in claim 5, or its progeny or tissue [having identical properties] that conserve said DNA which was introduced.

20. (Amended) [A] An isolated nucleic acid molecule comprising a sequence of nucleotides encoding, or complementary to[,] a sequence encoding, a plant flavonoid-5-glucosyltransferase (5GT).

22. (Amended) An isolated nucleic acid molecule according to claim 21, comprising a nucleotide sequence, or nucleotide sequence complementary to a nucleotide sequence as set forth in SEQ ID NOs: 7-10 or 12, or having at least 50% [homology] a sequence identity thereto.

Attachment to Reply and Amendment dated April 3, 2002

Marked-up Claims 1-6, 10, 11, 16-20 and 22-24

23. (Amended) An isolated nucleic acid molecule which:

(i) encodes a 5GT of plant origin; and

(ii) hybridizes under conditions of 5 x SCC and 50°C with a nucleotide sequence as set forth in SEQ ID NOs: [7-10 and 12] 1, 3, 5, 7 or 11, or to a complementary strand thereof.

24. (Amended) An isolated [gene] DNA coding for a protein having activity that transfers a glycoside to the 5 position of a flavonoid, wherein said [gene] DNA encodes a protein having

an amino acid sequence selected from the group consisting of [those shown in] SEQ ID NOs: [7-10 and 12] 2, 4, ,6, 8 and 12, or

an amino acid sequence which is at least 50% [homologous with] identical to an amino acid sequence [as shown in] of SEQ ID NOs: [7-10 and 12] 2, 4, 6, 8 or 12, [and] or

[an amino acid sequence which will hybridize] wherein said DNA sequence hybridizes with the complementary strand of [an amino acid sequence as shown in] a DNA sequence of SEQ ID NOs: [7-10 and 12] 1, 3, 5, 7 or 11.